

**REMARKS**

Claims 1-16, 18-44, 46-50 and 52-61 are currently pending in this application. Claims 28, 31-35, 38-39, and 43-44 are amended herein. Claims 1-16, 18-27, 29-30, 46-47, 49, 52-56 and 60-61 are canceled by way of this response. Upon entry of this response with amendments, claims 28, 31-44, 48, 50 and 57-58 will be pending. Support for amended claim 28 can be found throughout the application as originally filed, *inter alia*, on page 3, lines 4-29. Support for amended claims 43 and 44 can be found throughout the application as originally filed, *inter alia*, on page 10, line 34 extending to page 11, line 8. Accordingly, Applicants submit that no new matter is introduced into the application by way of the present claim amendments. Also, no new issues are presented by claim amendments because recitations of the amended claims have been present in the claims prior to the Office Action.

**Restriction Requirement**

Applicants respectfully continue to disagree with the restriction requirement for the reasons set forth in Applicants' responsive submission dated June 14, 2004. However, in the interests of expediting prosecution, Applicants are canceling withdrawn claims 1-16, 18-27, 52-56 and 59 without prejudice or disclaimer as to the subject matter therein. Applicants respectfully reserve the right to pursue the subject matter of these canceled claims in one or more divisional or continuation applications.

**Change in Taxonomic Designation of *Cimicifuga racemosa***

Applicants respectfully note that the taxonomic designation of *Cimicifuga racemosa* has been changed in the literature to *Actaea racemosa*. Applicants submit herewith as Appendix A a Danish article, Else Als, *Actaea druemunke og sølvlys*, Haven, no. 10, October 2004. Applicants further submit herewith as Appendix B an English translation of the most relevant parts of the article, evidencing the change in the taxonomic designation of this species from *Cimicifuga racemosa* to *Actaea racemosa*.

Applicants respectfully request that the Examiner indicate to Applicants whether it is necessary to amend the claims of the instant application to reflect this change in taxonomic designation.

## **Rejections**

### *Rejections under 35 U.S.C. § 112, 2<sup>nd</sup> Paragraph*

Claims 28-44, 46-50, 57, 58 and 61 were rejected under 35 U.S.C. § 112, 2<sup>nd</sup> paragraph as allegedly failing to particularly point out and distinctly claim the subject matter regarded as the invention. The Office Action states that the use of the phrase “or at least one derivative of such substances” in claims 28 and 61 is unclear. The Office Action also questions the meaning of “comprising substances” in claims 28 and 61. Furthermore, the Office Action suggests the deletion of the term “included” in claims 28 and 61.

Applicants respectfully disagree and continue to maintain that all the rejected claims were definite because they readily apprised persons skilled in the art of the metes and bounds of Applicants’ claimed invention. However, in the interests of expediting prosecution, Applicants have amended the text of claims 28, 43 and 44. Applicants have canceled claims 29, 30, 46, 47, 49, 60 and 61 herein, rendering moot all rejections of these claims. Accordingly, Applicants’ remarks will be directed to claims remaining in the application. Applicants submit that the amended text of claims 28, 43 and 44, and the pending rejected claims depending therefrom (i.e., claims 31-42, 48, 50, and 57-58), satisfies the requirements of 35 U.S.C. § 112, 2<sup>nd</sup> paragraph. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 28, 31-44, 48, 50 and 57-58 under 35 U.S.C. § 112, 2<sup>nd</sup> paragraph.

### *Rejections under 35 U.S.C. § 112, 1<sup>st</sup> Paragraph*

#### *Written Description*

Claims 28-44, 46-50, 57, 58 and 61 were rejected under 35 U.S.C. § 112, 1<sup>st</sup> paragraph, as allegedly “containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.” *See* Office Action, Page 3, lines 16-19. The Office Action states that the “disclosure has no description of the claimed invention”; the “Examiner could not find support for ‘curing’ or ‘relieving’”; and queries “Which substances?” *See* Office Action, page 4, lines 3-5.

Applicants respectfully disagree and traverse this rejection. Applicants continue to maintain that their disclosure satisfied the written description requirement of claim 28, and the remaining rejected claims, dependent from claim 28, prior to the amendment herein. Skilled artisans familiar with the disclosure would have readily realized that Applicants possessed the subject matter of those claims at the time the application was filed.

Nonetheless, in the interest of expediting prosecution, Applicants have amended the text of claim 28 to remove the recitations of “curing”, “relieving”, and “substances.” Applicants submit that the rejection of claims 28, 31-44, 48, 50, and 57-58 based on the recitation of the terms “relieving”, “curing” and “substances” is rendered moot. Applicants submit the application as filed provides written description for all other pending claims. Applicants have already identified support for the amended claims in this submission. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 28, 31-44, 48, 50 and 57-58 under 35 U.S.C. § 112, 1<sup>st</sup> paragraph.

#### *Enablement*

Claims 28-44, 46-50, 57, 58 and 61 were rejected under 35 U.S.C. § 112, 1<sup>st</sup> paragraph, as allegedly “containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.” See Office Action, Page 3, lines 16-19. The Office Action sets forth eight (8) factors to be considered in determining whether a disclosure meets the enablement requirement, as articulated in *In re Wands*. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). According to the Office Action, “it is the Examiner’s position that one skilled in the art could not practice the invention without undue experimentation.” See Office Action, page 4, lines 12-13.

Applicants respectfully disagree and traverse this rejection.

It is well established under 35 U.S.C. § 112 ¶ 1, that “[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.” (*United States v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1986)). The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is

undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976), MPEP § 2164.01. As stated in the Office Action, the factors to be considered in determining whether a disclosure would require undue experimentation include: “(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability of the art, and (8) the breadth of the claims.” *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d, 1400, 1404 (Fed. Cir. 1988).

Applicants respectfully submit that the application, considered as a whole, satisfies each of these factors, as exemplified by specific portions of the specification discussed below.

*Enablement for Making *Cimicifuga racemosa* Compositions used in the Claimed Methods*

Applicants submit that the specification, as originally filed, provides adequate enablement to allow one skilled in the art to make the *Cimicifuga racemosa* compositions used in the claimed methods without undue experimentation. More particularly, amended claim 28 recites the use in the claimed method of “an extract of *Cimicifuga racemosa*, said extract obtainable by vortexing *Cimicifuga racemosa* material in an aqueous solution.” Applicants submit that the specification as a whole, including example 1, on page 15, line 23 extending to page 16, line 6, provides detailed guidance enabling one skilled in the art to produce the *Cimicifuga racemosa* compositions used in the claimed methods. In particular, example 1 teaches that a standardized *Cimicifuga racemosa* material as for example provided by Finzelberg AG, Germany (catalogue number 0472312 or 0472340) was used for extraction purposes. The desired extraction solution was made from 100 mgs of *Cimicifuga racemosa* material and 1660 ml of sterile water, which was vortexed and then kept at room temperature for 30 minutes. Example 1 also provides dosing amounts used in the murine models of the specification.

*Enablement for Using *Cimicifuga racemosa* Compositions in the Claimed Methods*

Applicants submit that the specification, as originally filed, provides adequate enablement to allow one skilled in the art to use the *Cimicifuga racemosa* compositions in the claimed methods also without undue experimentation. More particularly, amended claim 28 recites “[a] method for treating an estrogen deficient woman who suffers from breast cancer, or

has a risk of recurrent breast cancer, or has a risk of developing breast cancer, wherein said woman demonstrates symptoms of estrogen deficiency...” Applicants submit that the teachings of the specification, considered in its entirety, and particularly examples 2, 3, 4 and 5 provide an enabling disclosure allowing one of skill in the art to use the *Cimicifuga racemosa* extracts in the claimed methods, as is explained in greater detail below.

#### A. Diagnosis of Estrogen Deficiency

The Office Action states that “[i]n order to practice the claimed invention commensurate in scope with the instant claims, the skilled artisan would have to first determine patients in need of said relieving or curing. However, the skilled artisan would be unable to determine said patients in need of said relieving or curing without further guidance.” See Office Action, Page 6, lines 13-16.

Applicants have amended the text of claim 28 to substitute the term “treating” for the phrase “relieving or curing symptoms.” However, Applicants respectfully disagree with the above-quoted statement from the Office Action as it applies to the recitation of “treating”, “relieving” or “curing” in the claims. The specification on page 10, line 34 extending to page 11, line 8, discloses numerous estrogen deficiency-conditioned symptoms or diseases which include menopausal symptoms; dermatological disorders such as aging of the skin, wrinkles, dry skin and other estrogen deficiency related dermatological disorders; dryness of mucous membranes; brain related diseases such as Alzheimer’s and including other types of dementia; bone and joint related diseases such as osteoporosis, osteochondrosis, osteoarthritis, rheumatoid arthritis, healing of bone fractures, and reduction of skeletal fractures; vaginal estrogen deficiency including dyspareuni, coronary heart diseases such as arteriosclerosis; and diseases such as hyperlipidemia and hypercholesterolemia.

Applicants submit that the diagnosis of an estrogen deficiency-related disease or disorder (including those set forth *supra*) is within the abilities of a skilled person, such as a physician, and that furthermore a diagnosis of an estrogen deficiency-related disease or disorder is generally made by a skilled physician. Accordingly, Applicants submit that the detection of an estrogen-deficiency related disorder is enabled, based on Applicants’ disclosure, the predictability of the art, the knowledge in the art, and the relative skill of those in the art.

### B. Determination of Physiological Estrogen Effects

It was also stated in the Office Action that the application lacks examples or test data *in vivo* or *in vitro* to support all the claimed methods. See Office Action, page 6, lines 2-3. Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations, which include the presence or absence of working examples. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d, 1400, 1404 (Fed. Cir. 1988). Additionally, Applicants have provided numerous working and prophetic examples that have applicability to the enablement of the claimed invention. Some of these examples are based on murine models.

Applicants submit that the skilled artisan is enabled, without undue experimentation, by the specification to determine whether a given *Cimicifuga racemosa* extract, produced in accordance with Applicants' teachings, is capable of providing physiological estrogen effects. The specification, on page 7, line 19 extending to page 8, line 3, provides a recitation of physiological effects that are produced by estrogen. The specification, on page 8, lines 5-14, identifies one of the physiological effects that is a useful indicator of estrogen-like effects of a substance by stating that

[i]t will be obvious for the person skilled in the art to use one of the above-mentioned physiological estrogen effects as a measure of estrogen-like effect for a substance. One of these physiological effects, the stimulation of uterine growth, have been chosen in the present technical teachings (examples 1-4). Thus, in a preferred embodiment of the invention the physiological estrogen-like effect is uterine growth as determined by an increase in uterine weight compared to controls after administration of the substance to ovariectomized female athymic nude mice. That is, a physiological estrogen-like effect is uterine growth as determined by an increase in mean uterine weight compared to controls of at least 0.1 g after administration of the substance to ovariectomized NMRI female athymic nude mice for 8 days.

Additional disclosure enabling such a skilled artisan is provided at page 13, line 25 extending to page 14, line 25.

The specification further describes, in Example 1, the measurement of physiological estrogenic effects, specifically uterine weight, in response to orally administered *Cimicifuga*

*racemosa* extract in adult ovariectomized NMRI female athymic nude mice. According to the teachings of the specification, the *Cimicifuga racemosa* extract of Example 1 was chosen to simulate the daily recommended dose, and had an *in vivo* effect on mouse uterine weight which was comparable to that seen following estradiol treatment. Example 5 provides additional prophetic teachings directed to experimental models for testing differential estrogenic effects of substances.

The specification also provides detailed descriptions of experiments that are useful in determining whether a given substance influences the growth of human breast cancer xenografts transplanted in mice. For example, the specification in Examples 2 and 3 examines the effect of orally administered *Cimicifuga racemosa* extract on tumor development and growth of both the MDA-MB-232 and MCF-7 human breast cancer xenografts, respectively. In each of these examples, the *Cimicifuga racemosa* extract had no effect on growth of the estrogen and progesterone receptor negative MDA-MB-231, and the estrogen dependent MCF-7, human breast cancer xenografts.

The specification also provides guidelines for dosing concentrations of *Cimicifuga racemosa* extracts. For example, the specification on page 3, lines 22-29, states that doses of the extract may be from, e.g., 1 mg to 20 mg daily on the basis of the extract, such as 2-3 mg twice daily for a woman.

Based on these disclosures, Applicants submit that the teachings of the specification enable one skilled in the art to practice the claimed invention commensurate with the scope of the claims. For example, the specification provides adequate teachings enabling one skilled in the art to isolate *Cimicifuga racemosa* extracts. The specification further provides teachings allowing one of skill in the art to determine whether a given *Cimicifuga racemosa* extract has estrogen-like effects. In addition, the specification provides teachings allowing one skilled in the art to determine whether a given *Cimicifuga racemosa* extract influences the growth of human breast cancer xenografts transplanted in mice. Additionally, the specification provides dosing guidelines for the concentration of *Cimicifuga racemosa* administered to patients. Applicants submit that these teachings are more than adequate to enable one skilled in the art to obtain *Cimicifuga racemosa* extracts and utilize those extracts in the claimed methods of the invention, commensurate with the full scope of the claims, without engaging in undue experimentation.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 28, 31-44, 48, 50, and 57-58 under 35 U.S.C. § 112, 1<sup>st</sup> paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

## **CONCLUSION**

An indication of allowance of all claims is respectfully solicited. Early notification of a favorable consideration is respectfully requested. In the event any issues remain, Applicants would appreciate the courtesy of a telephone call to their counsel to resolve such issues and place all claims in condition for allowance.

Respectfully submitted,

HUNTON & WILLIAMS LLP

Dated: January 10, 2005

By: 

Robert C. Lampe III  
Registration No. 51,914  
Stanislaus Aksman  
Registration No. 28,562

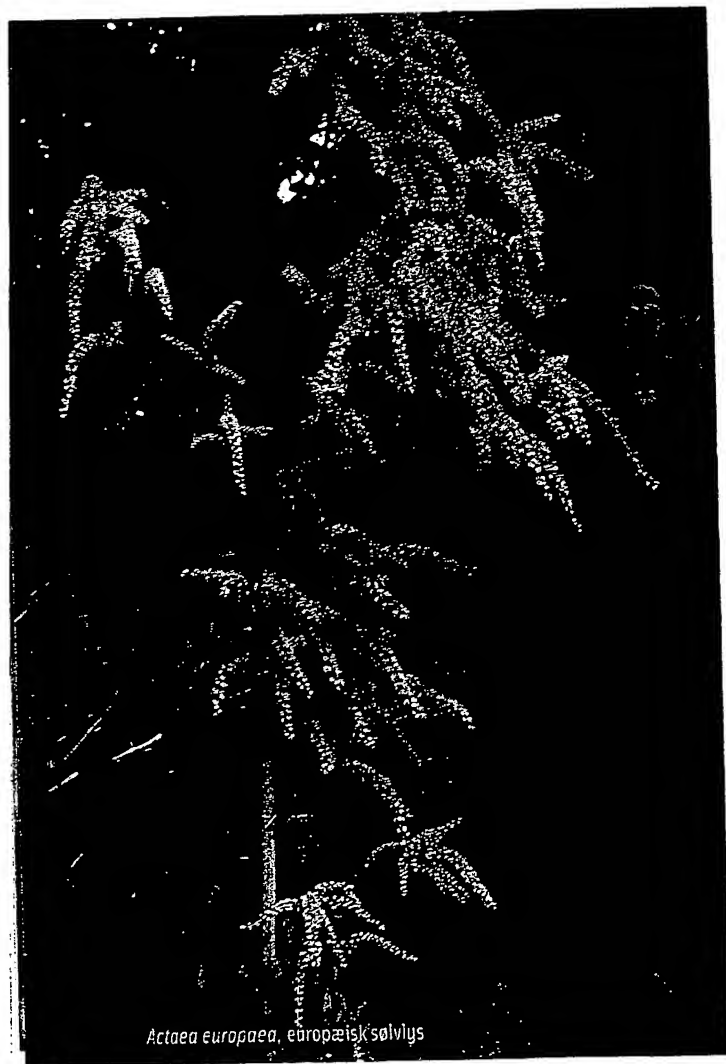
HUNTON & WILLIAMS LLP  
1900 K Street, N.W.  
Suite 1200  
Washington, D.C. 20006-1109  
Telephone: (202) 955-1500  
Facsimile: (202) 778-2201



*Actaea*, druemunke er en slægt med 4-5 arter, og sådan har det været i mere end 200 år, men i 1998 skrev tre engelske botanikere en afhandling, hvor de på basis af bl. DNA-analyser indlemmer hele *Cimicifugaslægtens* 15-20 arter tilligemed en næsten ukendt slægt, *Souleia*. Man kunne jo med en vis ret hævde, at det egentlig burde være den lille slægt, *Actaea*, som skulle indlemmes i den store slægt, *Cimicifuga*, men her er det så omvendt, at den lille fører

Tekst og foto Else Als skribent

# Actaea druemunke og sølvlys



*Actaea europaea*, europæisk sølvlys

Allerede botanikens fader, Carl von Linné, var inde på for 250 år siden, at sammenligne *Actaea* og *Cimicifuga*, idet han allerede i 1752 navngav slægten *Cimicifuga* ud fra en plante med flere (faktisk fire) frugtblade, *C. foetida*, hvorefter han lidt senere ombestemte sig og flyttede arten til *Actaea*, *Actaea cimicifuga*.

Linné mente, at de få arter med bær var *Actaea*, og at de arter med tørre frøkapsler var *Cimicifuga*. Senere bestemte han, at de arter, som havde mere end én frøkapsel pr. blomst, var *Cimicifuga*-arter.

Linné kom igen i 1767 på andre tanker og definerede nu de to slægter på frugtbladstallet: 1 frugtblad (*Actaea*), flere frugtblade (*Cimicifuga*) og anså derfor ikke frugttype-forholdet bær/bægkapsel som værende det afgørende.

## Stor navneforvirring

Sådan var bestemmelsen, indtil den britiskfødte, Thomas Nuttall i 1818 blandede sig og dekreterede, at arter med bær var *Actaea*, og arter med frøkapsler var *Cimicifuga*, hvilket medførte, at nogle arter af de to slægter igen til stor forvirring skiftede plads.

I de senere år har botanikere ført en del latinske plantenavne tilbage til de oprindelige til Linnés system, fordi der i tidens løb var sket for mange botaniske justeringer, så det hele var blevet til stor forvirring.

Ikke kun plantenavne; men hele slægter sådan som *Actaea* og *Cimicifuga*, har man i dag ført tilbage til Linnés system, men de er dog blevet i familien, *Ranunculaceae*. For det er også sket, at nogle planter er ført i helt andre familier.

## DNA-analyser sætter tingene på plads

Moderne undersøgelser ved hjælp af DNA viser, at der er så stor lighed mellem disse to slægter, *Actaea* og *Cimicifuga*, at det er besluttet, at de fra 1998 er *Actaea*. Som almindelig havemand kan man mene, at de gamle *Actaea* er ret små planter med korte, tætte aks og bærfrugter, mens de nye *Actaea* er op til to-tre gange større planter med lange, smalle aks og tørre frø i kapsler, og som sådan ret forskellige.

Blomsterne er hvide eller hvidlige hos begge typer og som sådan de mest ens ligheder. Men sektion *Souleia* har lyserøde



*Actaea simplex* 'Brunette', sølvlys

staminodier (rudimentære støvblade uden støvknapper), mens sektion *Cimicifuga* har gule til orange staminodier.

DNA-analyserne fortæller selvfølgelig noget helt andet, at de er så meget lig hinanden på mange punkter, så de nu er smeltet sammen til *Actaea*.

Der vil blive adskillige fagbøger/lorabøger, som skal opdateres i de kommende år. Efter denne revision indeholder *Actaea* nu 28 arter, hvoraf kun de mere kendte arter vil blive beskrevet her.

### God staudef til fugtig jor

*Actaea*, druemunke og sølvlys træffes i naturen mest i skove, i fugtig og god skovjor, hele den nordlige halvkugle rundt. Det er havernes gode staudef med kraftige, træede, rhizomagtige jordestængler, der for sølvlys vedkommende har en tendens til at gro op ad jordef.

Højden varierer fra 50 cm til op mod to meter med gode, kraftige, næsten træede stængler, der står helt uden opbinding.

Bladene er både grundstillede og med stængelblade på den grenede stængel, og de er typisk for mange af ranunkelfamiliens slægter 3-delte og meget indskårne, siddende på ret lange bladstilke.

Blomsterne er hvide, siddende i et kort, tykt aks (druemunke) eller hvide, cremefarvede, hvid- el. gulgrønne (sølvlys), siddende i smalle, ofte grenede, lange blomsteraks (sølvlys). Enkelblomsterne har fire små bægerblade, som hurtigt drysser af, fire små kronblade, talrige udstående støvdragere, som resulterer i et kødfuldt bær, hvor frøet sidder (druemunke). Hos sølvlys er frugten en frø kapsel med tørre frø. Blomstring juli-oktober.

Både druemunke og sølvlys er dejlige, hårdføre staudef, som tåler vinterens skiftende frøst og tø. Derimod tåler de ikke at stå for tørt, hvilket man hører om for alle arterne, at de kommer fra fugtige steder, oftest i skove og gerne i halvskygge, som de skovens planter de er.

### Formeres i det tidlige forår

Vil man formere *Actaea*, sker det bedst tidligt forår, når man kan se de nye, rødlige skud. På den tid deler man klumpen og kaster de mest tørre, midterste rødder væk, da de bare tager

plads op. De yderste skud er alligevel de mest friske og grobare. Man kan da også så både de modne bær og de tørre frø kapsler, men for de sidste tager det lang tid, op til fem år, inden planterne er blomsterdygtige.

### Giftig men ufarlig

Druemunke og sølvlys indeholder et giftstof, anemonol, som er hudirriterende på den måde, at man skal lade være med at røre ved de friske planter i stærkt sollys, hvis man har tendens til den slags hudproblemer.

Druemunke har også været anvendt i folkemedicinen mod astma og hudsygdomme. Selv om bærrerne er lidt giftige, er de ikke farlige, simpelthen fordi de smager grimt og skarpt, hvis småbørn skulle forgribe sig på dem.

### Arterne

*A. arizonica* (*Cimicifuga arizonica*), sølvlys, kommer naturligvis fra USA's stat, Arizona. Det er en 70-150 cm høj staudef, som har opret, grøn og glat stængel med 2 gange 3-delte blade med 9-45 cm lange blade. Akset indeholder mange cremehvide, små blomster.

*A. asiatica*, asiatisk druemunke, som er naturligt forekommende i Asien, i Kina, Korea og Japan, bliver 60-70 cm høj. De store grundstillede blade bliver ca. 0,5 meter lange pga. lange bladstilke. Blomsterakset er lille, tæt og op til 6 cm langt og resulterer i sorte, næsten runde 6 mm små bær. Den afblomstrede blomsterstand ser spøjs ud med rødlige, nåleformede, slidte støvdragere med de små sorte bær i toppen.

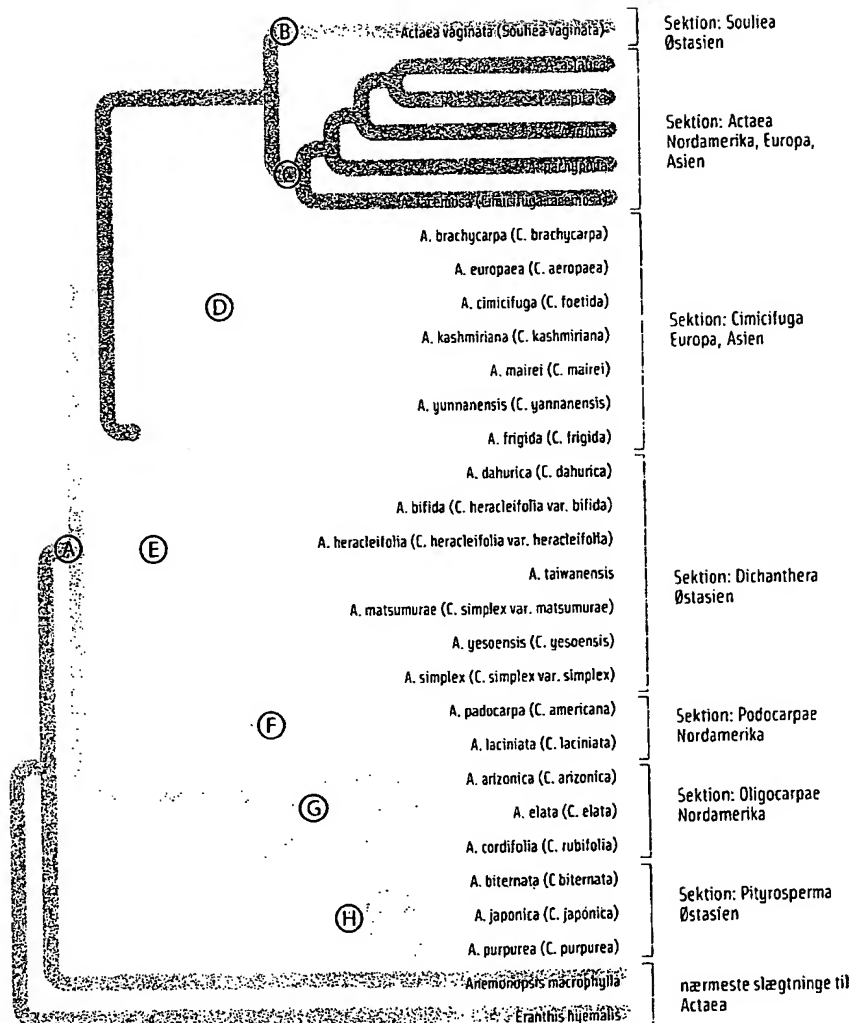
*A. cimicifuga* (*Cimicifuga foetida*), sølvlys, er hjemmehørende i Pakistan og Tibet, hvor den vokser i krat og skovlysninger i op til 4.000 meters højde. Det er en 1-2 meter høj, statelig staudef med de sædvanlige 3-delte blade. Det buede aks indeholder små gullige blomster, som sidder tæt i akset. Blomstring midtsommer.

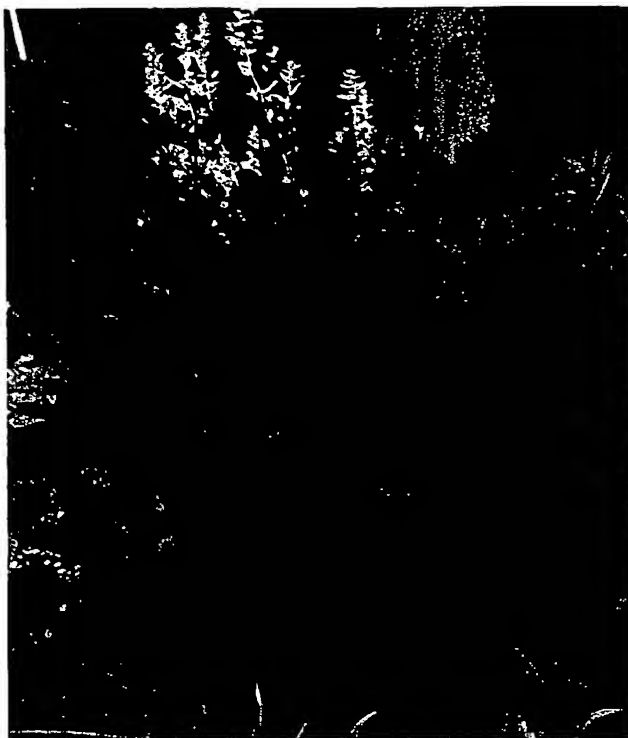
*A. cordifolia* (*Cimicifuga racemosa* var. *cordifolia*, *C. rubrifolia*), sølvlys, kommer fra USA's stater, Carolina og Tennessee. >

## STAMTRÆ FOR ACTAEA

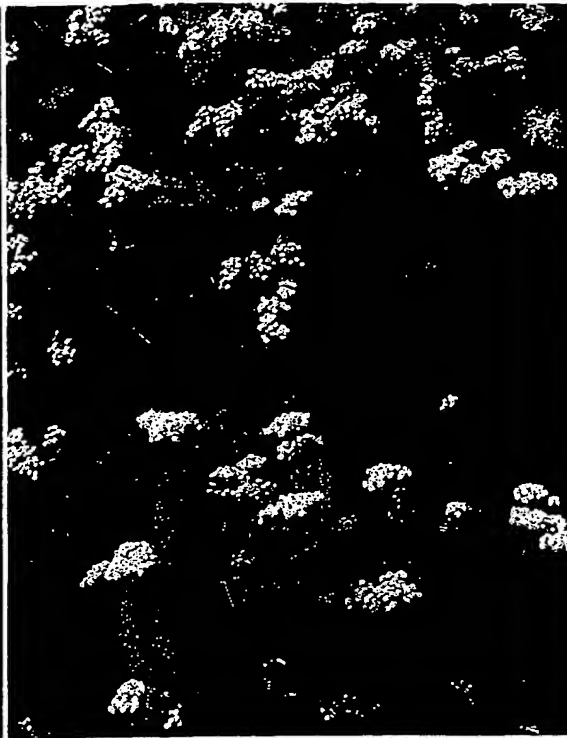
I denne nye klassifikation af slægten Actaea (som også omfatter arter, der tidligere havde slægtsnavnene *Souliea* og *Cimicifuga*), er nært beslægtede arter opdelt i sektioner. Selvom denne opdeling er baseret på både morfologiske og genetiske studier, har hver sektion mindst én synlig egenskab tilfælles og har et afgrænset geografisk udbredelsesområde.

- A. hovedgren, der adskiller Actaea fra dens nærmeste slægtninge
- B. lyserøde kronblade, blomsterstanden er uforgrenet
- C. kun én frugt per blomst, 4-8 hvide kronblade
- D. 2-4 gule eller orange kronblade
- E. 2-4 hvide kronblade
- F. 2 cremefarvede kronblade, 1 dækblad ved blomsterstilkens base
- G. kronbladenes stilke er meget korte, de yderste småblade har 5-7 bladstreng
- H. dækbladene er stort set deltaformede (triangulære)





*Actaea simplex* 'Variegata', brogetbladet sølvlys



*Actaea pachypoda*, hvid druemunke

➤ Det bliver en ret høj staude fra 1,25-2 meter med ret brede blade, der er 2 gange 3-delte og med småblade opad stænglen, som er hjerteformede i spidserne. Akset indeholder cremefarvede små blomster eller cremefarvet-brunlige, der får dem til at se ud til at være på vej til afblomstring. Blomstring i august.

*A. duhurica* (*Cimicifuga dahurica*), asiatisk sølvlys, stammer fra Asien, fra Sibirien og Japan. Det er en høj staude, som kan blive over 2 meter høj med blade, som er 2 el. 3 gange 3-delte. De lange, grenede og smalle aks indeholder rent hvide, små blomster, dvs. det gør hanblomsten, mens hunblomsten er mere uanselig med endnu mindre blomster, som gør den mindre dyrkningsværdig. Blomstring i august.

*A. europaea* (*Cimicifuga europaea*), europæisk sølvlys, findes i Mellemeuropa østover fra Tjekkiet til Bulgarien. Stænglen er glat, 40-100 cm høj med store blade, som er 2 el. 3 gange 3-delte. Akset er langt og smalt med gulgrønne småblomster i det grenede aks.

*A. japonica* (*Actaea acerina*, *Cimicifuga japonica*), japansk sølvlys, kommer naturligvis fra Japan, som navnet siger. Det er en ca. 1,50 meter høj plante med grundstillede almindelig eller 2 gange 3-delte, skarpt indskårne blade, som er ca. 0,5 meter lange. Blomsterakset er kun lidt forgrenet og ret fyldigt med mange små hvide blomster. Akset er flot, opret og langt. Blomstring august-september.

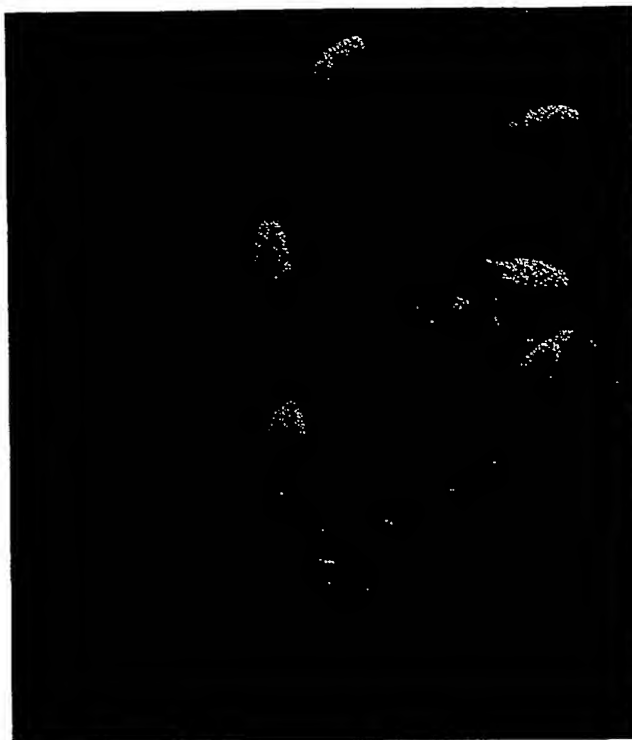
*A. matsumurae* (*Cimicifuga simplex* var. *matsumurae*), er ved fusionen med *Actaea* blevet "ophøjet" til en art i stedet for en sølvlys-varietet. Det er en høj og flot plante på 90-125 cm med blomstring i august-september. Det lange aks er fyldt med hvide blomster. 'White Pearl', buet aks af hvide blomster, sept.-okt., 90-150 cm, er en særlig flot sort med tykt, hvidt, buet aks.

*A. pachypoda* (*A. alba*), hvid druemunke, som stammer fra det østlige USA, ligner meget den mest almindelige *A. spicata*. Bladene er 2 gange 3-delte, takkede blade, og højden rapporteres at være op til 90 cm, der dog hos os oftest er 50-60 cm. Blomsterstanden indeholder et kort hvidt aks, hvorimod stænglen afslører, at den er helt sin egen, med en særpræget, mørkerød stængel. Når blomsterne er afblomstrede, er det en meget smuk kontrast til de opalhvide bær på også mørkerøde blomsterstilke. Heldigvis står de sådan i endog meget lang tid, en flot dekoration i haven. Blomstring i juli.

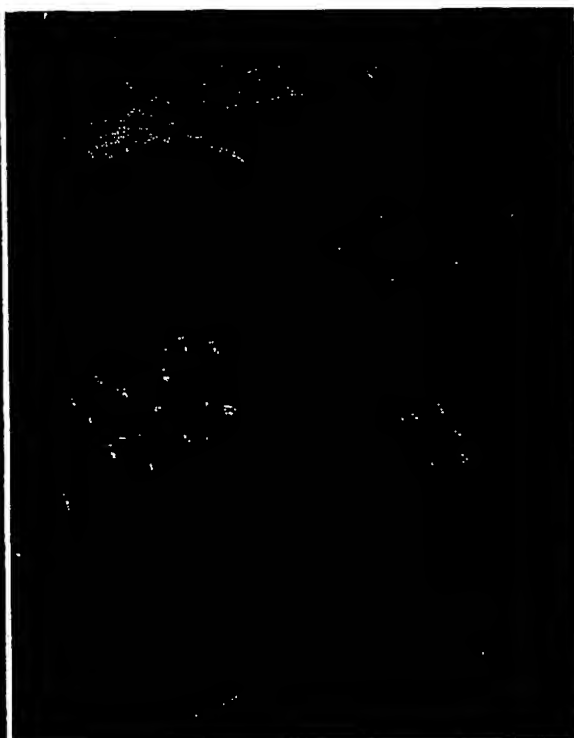
*A. podocarpa* (*Cimicifuga americana*), amerikansk sølvlys, kommer fra Pennsylvania og sydpå til Georgien, USA, hvor den gror i fugtige skove. Planten, 60-180 cm høj, kan blive op til 2 meter med 2 el. 3 gange 3-delte blade. Akset er flot, opret, delt i 3 aks i toppen og tæt fyldt af små hvide blomster. Planten er nærtstående til *A. racemosa*, men er fri for dennes ramme lugt.

*A. racemosa* (*Cimicifuga racemosa*), sølvlys, er amerikaner fra de nordøstlige stater og ind i det sydlige Canada. Det er den tidligst blomstrende sølvlys, som allerede er i blomst i juli. De stive, grønne stængler rejser sig 125 cm fra et tæt buskads af 60-70 cm høje 2 el. 3 gange 3-delte blade. Med tiden gror rødderne træagtigt op af jorden, og når man kan se, at midten bliver bar, er det på tide at grave op og tage de mest friske skud i kanterne fra og plante igen, ellers risikerer man, at planten enten bliver mindre eller helt forsvinder. Det tager dog en del år, før man behøver at dele og nyplante igen. Blomsteraksene er talrige, men spinkle med kridhvide, stærkt lugtende blomster.

*A. rubra*, (*A. spicata* var. *rubra*), rød druemunke, er amerikaner fra det vestlige Amerikas stater fra Alaska til New Mexico. Planten er 50-70 cm høj, med 2 gange 3-delte blade. Blomsterakset er som hos "de gamle" *Actaea*, et tæt, kort aks med små hvide blomster, men frugten er endog meget flot med skinnende, ➤



*Actaea spicata*, almindelig druemunke



*Actaea rubra*, rød druemunke

➤ store blodrøde bær, op til 1 cm store i diameter, så tunge, at når de er modne, står akset i en yndefuld bue. Moden i september.

*A. simplex* (*Cimicifuga simplex*, *C. ramosa*), grenet sølvlys, er den bedst kendte sølvlys, den der er udviklet sorter fra, men bedre kendt under navnet *C. ramosa*. Arten stammer fra Kamtschatka, Kurilerne og Sakhalin i Japan. Det er den typisk høje staude med hvidlige blomster i let buede aks i oktober. Det er derimod sorterne, man ser i haverne, smukke planter i et brus af blade, og specielt de sorter med mørkt løv til hvide blomster, skiller sig markant ud, selv om løvet falmer lidt sent i blomstringen:

#### *Actaea simplex*-sorter

'Atropurpurea', sortrødt løv, cremehvide blomster, 180 cm.

'Brunette', brune stængler og kønt, sortrødt løv, grundstillede blade, fylldigt aks af hvide blomster i sep. - okt., 125 cm.

'Elstead', purpurbrune knopper, hvide blomster.

'Purpurea', purpurbrune stængler og blade, hvide blomster, sep.-okt., 175 cm.

'Variegata', spinkel plante, hvidbrogede blade i begyndelsen, aug., 1 m

*A. spicata*, almindelig druemunke, er den mest almindelige druemunke-art, hvor man på blomstringstidspunktet har svært ved at afgøre, hvilken af de 4 arter druemunke, det er, fordi blomsterstanden er ens hos alle 4 druemunke. Det er først, når frøstanden, bærret, modner, at man sikkert kan se, at små sorte bær og rødlig rester af blomsterakset er *A. asiatica*, røde blomsterstilke og hvide bær er *A. pachypoda*, mørkerøde bær er *A. rubra* og store sorte bær er *A. spicata*.

Almindelig druemunke findes over stort set hele Europa, også i Danmark, desuden østover helt til Kina, hvor den alle steder gror i skove i fugtig humusjord. Planten er 30-60 cm høj i naturen, i haverne nærmest det sidste. Stænglen er grenet med typiske,

takkede 2 gange 3-delte blade og korte, oprette, tæt blomstrede aks af små hvide blomster, som har 4 små ret hurtigt affaldende bægerblade, 4 små kronblade og utallige, udstående støvdragere. Frugten, bærret, er ca. 1 cm stort og skinnende sort.

*A. vaginata*, (*Souliea vaginata*), stammer fra det vestlige Kina, fra Kansu og Yunnan-provinserne, hvor den gror i skove. Planten har kraftige rhizomagtige rødder og bliver sammenlignet med både *Isopyrum* og *Cimicifuga*. Stænglen er 60-80 cm høj, og i toppen sidder en klase med ret store, hvidlige 5-tals blomster, meget lignende sølvlysblomster. Botanikerne, som har sammenføjet *Cimicifuga* med *Actaea*, har set, at den tidligere *Souliea vaginata* har så mange ligheder, at den også er blevet inddraget. Planten er dog nærmest ukendt, idet ingen florabøger omtaler den. Kun en over hundred år gammel fransk, botanisk journal omtaler den og desværre uden illustration.

Tak til lektor Jørgen Jensen, Botanisk sektion, Den Kgl. veterinær- og Landbohøjskole for faglig gennemlæsning

*Patent Application No. 10/030,971*  
*N. Brunner et al.*  
*January 10, 2005*  
*Attorney Docket No. 60730.000002*

**Appendix B**

**This Page is Inserted by IFW Indexing and Scanning  
Operations and is not part of the Official Record**

**BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☐ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☐ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☐ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** \_\_\_\_\_

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.**

Already 250 years ago the father of botany, Carl von Linné, touched on the idea of comparing *Actaea* and *Cimicifuga*, naming already in 1752 the genus *Cimicifuga* with inspiration from a plant having several (actually four) carpels, *C. foetida*, whereupon, a little later he changed his mind and moved the species to *Actaea*, *Actaea cimicifuga*.

5 Linné was of the opinion that the few species bearing berries were *Actaea*, and that the species bearing dry capsules were *Cimicifuga*. Later he decided that the species having more than one capsule per flower were *Cimicifuga* species.

In 1767 Linné, once again, changed his mind and then defined the two genera based on the number of carpels: 1 carpel (*Actaea*), several carpels (*Cimicifuga*), and  
10 thus did not consider the fruit-type relationship berry/follicle to be decisive.

### **Great name confusion**

This was what was determined until 1818 when Thomas Nuttall of British origin interfered and ordered that species bearing berries were to be *Actaea*, and species  
15 bearing capsules were to be *Cimicifuga*, which meant that some species of the two genera changed places, once again causing great confusion.

During recent years botanists have carried a number of Latin plant names back to the original names of Linné's system because, in the course of time, many botanical adjustments had been made, which meant that it had all turned into too much  
20 confusion.

Not only plant names, but entire genera such as *Actaea* and *Cimicifuga* have today been carried back to Linné's system, although they have been kept in the family, *Ranunculaceae*. However, there are also examples of some plants being carried to completely different families.

25

### **DNA analyses put things in place**

Recent studies carried out by means of DNA show that there is such a strong resemblance between the two genera, *Actaea* and *Cimicifuga*, that it has been decided that from 1998 they are to be *Actaea*. A common gardener may think that the old  
30 *Actaea* are quite small plants with short, closely situated spikes and baccate fruit, whereas the new *Actaea* are up to two to three times larger plants having long, slim spikes and dry seeds in capsules, and as such they are quite different.



The flowers of both types are white or whitish and as such the most striking resemblance. But the section *Souliea* has pink staminodies (rudimentary androecium without anthers), whereas the section *Cimicifuga* has staminodies ranging from yellow to orange.

5 Obviously, the DNA analyses show something quite different, that they are so similar to each other in many aspects that they have now become fused into *Actaea*.

Several specialist books/handbooks of flowers will have to be updated in the years to come. After this revision, *Actaea* now covers 28 species of which only the better known species will be described here.

10

*A. racemosa* (*Cimicifuga racemosa*), black cohosh, is native to America in the north-eastern states and spreading into southern Canada. It is the first black cohosh to bloom as it is in bloom already in July. The stiff, green stems raise 125 cm from a thick shrubbery of 2 or 3 times tripartite leaves with a height of 60-70 cm. In the  
15 course of time, the roots will grow from the soil in a treelike manner, and when it is perceptible that the middle becomes bare, it is time to dig up the roots and remove the freshest shoots at the edges and replant, otherwise there is a risk that the plant will either become smaller or completely disappear. A number of years will pass, however, before it is necessary to divide and replant. Spikes are abundant but thin  
20 with chalk-white, strongly smelling flowers.